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# Beyond DSM and ICD: introducing “precision diagnosis” for psychiatry using momentary assessment technology

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In medicine, a diagnostic system should ideally be mechanism-based rather than symptom-based. Although attempts to create diagnostic entities in psychiatry that are based on specific *biological* mechanisms have failed (1), new evidence suggests that an alternative mechanistic approach, based on *mental* mechanisms, can be readily implemented in psychiatry, complementing the widely criticized categorical systems of DSM and ICD.

Below, we describe the contours of a novel system of diagnosis in psychiatry based on: a) the need for a more individualized approach, based on causal influences in symptom circuits (“precision diagnosis”); b) the need to take into account the fact that symptoms reflect responses to context (“context diagnosis”); c) the need to take into account that syndromes develop over time and have recognizable stages of expression (“staging diagnosis”) (2); and d) the need for the diagnostic process to become collaborative rather than unidirectional, reflecting the first stage of collaboration between patient and professional, and the first stage of treatment.

The proposed diagnostic system is based on novel digital momentary assessment technology, which allows the patient to collect data on symptoms and contexts in the flow of daily life, from which detailed contextual symptom circuits can be constructed, that serve as a diagnostic and therapeutic tool, as well as an instrument to assess change.

## THE PRINCIPLE OF CONTEXTUAL PRECISION DIAGNOSIS

The main problem with psychiatric diagnosis is that groups identified by a common label, for example schizophrenia, in fact have little in common. The level of heterogeneity in terms of psychopathology, need for care, treatment response, illness course, cognitive vulnerabilities, environmental exposures and biological correlates is so great that it becomes implausible that these labels can provide much clinical utility.

In other areas of medicine, unexplained heterogeneity was addressed by the introduction of precision (or personalized) diagnosis. For example, blood pressure, plasma glucose, cardiac rhythm, electroencephalogram, muscle tone and other somatic outcomes can now be monitored in daily life, allowing for a diagnosis that yields individualized information about the pattern of *variation* of the parameter in question in

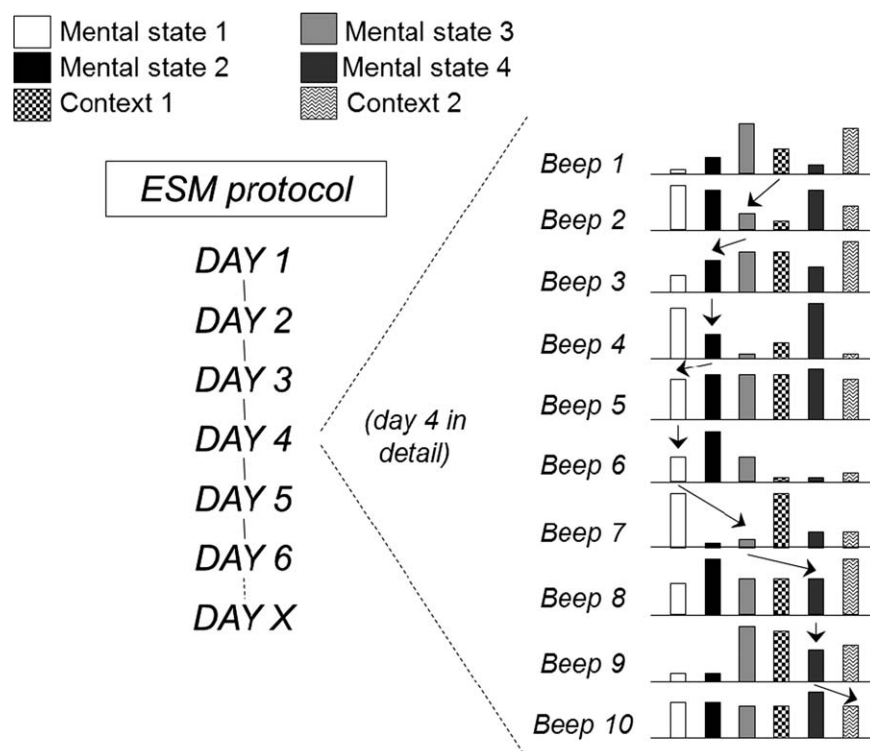
response to daily life circumstances. This diagnostic information is *precise*, as it reflects highly personal patterns of variation, and is *contextual*, as it traces variation related to daily life circumstances of, for example, stress, sleep, medication and life style. It is also *collaborative*, as the patient is actively involved in collecting and interpreting the diagnostic data. This not only enables precise indexing of treatment needs (diagnosis), but also precise monitoring of treatment response (prognosis). A similar system of contextual precision diagnosis may be useful in psychiatry.

## PRECISION: DIAGNOSING MENTAL CAUSATION IN SYMPTOM CIRCUITS

How can diagnosis based on psychopathology be similarly individualized? To date, the most commonly used attempt at individualization is based on assigning individuals to diagnostic categories, in combination with personalized ratings of psychopathology across different dimensions. In theory, this system of “dimensionalized categories” ought to yield acceptable precision, given that two individuals within the same diagnostic category will nearly always have different psychopathological profiles.

Recent research, however, indicates that this system is based on the false premise that symptoms always vary together as a function of a latent underlying dimension or category – which does not appear to be the case (3,4). Instead, it has been argued that mental “disorders” in fact may represent sets of symptoms that are connected through a system of causal relations, which may explain individualized co-occurrence of different symptoms (4,5). For example, the negative and positive symptoms of schizophrenia have largely independent courses (6), and etiological factors appear to operate at the symptom level rather than the diagnostic disorder level (7-9).

Therefore, there is increasing interest in how multiple symptoms in individuals arise not as a function of a latent construct, but as a function of symptoms impacting on each other, for example insomnia impacting on depressive symptoms (10) or on paranoia (11), depressive symptoms impacting on anxiety symptoms (12), affective disturbance giving rise to psychosis (13,14), negative symptoms predicting psychosis (15), and hallucinations impacting on delusions (16,17). Not only between-symptom dynamic relationships



**Figure 1** Momentary assessment with the Experience Sampling Method (ESM). At 10 random moments during the day, mental states (e.g., anxiety, low mood, paranoia, being happy) and contexts (stress, company, activity, drug use) are assessed. The arrows represent examples of prospectively analyzing the impact of mental states and contexts on each other over time.

have been described, but intra-symptom temporal dynamics resulting in *persistence* or, in momentary assessment technology terms, *momentary transfer* of symptoms have been observed. For example, intra-symptom dynamics over time, in the form of intra-symptom feedback loops, have been described in the area of psychosis, both at the momentary “micro-level” over the course of a single day in daily life (18), or over the course of months or years (19,20), under the influence of genetic and non-genetic risk factors (21-23).

The notion that traditional diagnostic categories and dimensions need to be transformed to represent the dynamics of symptoms impacting on each other over time in a model of mental mechanisms or mental causation is tantalizing. It implies that special methodology is required to collect repeated measures of symptoms over time in the flow of daily life, both at the momentary level and over more extended periods (24). This type of information allows for a detailed analysis and systematic presentation (25) of how symptoms impact each other (4,5,18).

## CONTEXT: DIAGNOSING ENVIRONMENTAL REACTIVITY

Although it is widely believed that mental disorders have their origin in altered cerebral function, disease categories

as defined in DSM and ICD do not map on to what the brain actually does: mediating the continuous flow of meaningful perceptions of the social environment that guide adaptive behaviour. The use of *ex-cathedra* static diagnostic categories appears distal from the neural circuits that mediate dynamic adaptation to social context.

Therefore, reformulation of the basic psychopathological unit towards capturing dynamic reactivity, modelled on the role of neural circuits in mediating adaptive functioning to social context, may be productive in the context of diagnosis. Momentary assessment technology phenotypes capturing dimensional variation in mental states in response to other mental states in the symptom circuit on the one hand, and to environmental variation on the other, are well placed to fill these requirements (Figure 1), resulting in a diagnosis that is both contextual and precise.

It is proposed that momentary assessments of contextual symptom circuits, using the Experience Sampling Method (ESM), will provide a fertile model for investigation of psychopathology, encompassing phenotypes at multiple levels of neurofunctional organization (26). For example, momentary assessment technology studies of exposure to early trauma in humans have yielded replicated evidence that early environmental exposures predict altered momentary response to stress in adulthood that increase the risk of mental disorder (27-29). There is a

suggestion that these ESM phenotypes of behavioural sensitization (30) can be linked to biological models of sensitization (31,32), thus suggesting that the momentary environmental reactivity may represent a key variable in linking mental and neurobiological phenotypes (33). Also, several ESM mental state measures have shown that connections between momentary mental states and environments are sensitive to genetic effects, not just in terms of heritability and familial resemblance (34,35), but particularly in terms of the genetics underlying environmental sensitivity (36-43), a mechanism referred to as gene-environment interaction.

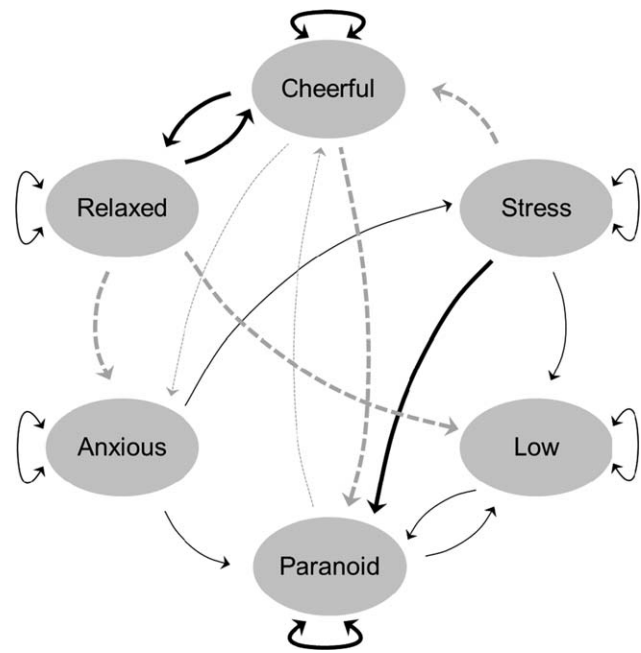
## EMPOWERMENT: A COLLABORATIVE DIAGNOSTIC PROCESS

In the momentary assessment paradigm of diagnosis as described above, patients collect their own data in daily life, and not only assist in observing variation in mental states, but also learn about daily environments likely to induce changes therein. Their experiences are assessed and translated in the diagnostic paradigm. For example, tracking aberrant salience can be explained as “let’s follow how you tend to put some issues under a magnifying glass”, or “let’s see what kind of environment helps you to generate positive affect”. This stimulates awareness and involves patients in making their own diagnosis, both at the level of psychopathology and at the level of functioning, relevant for both treatment and rehabilitation. During treatment, patients can directly observe how treatment impacts their dynamically varying mental states in response to environmental challenges in the flow of daily life. Patients thus become empowered to evaluate their own diagnosis and treatments in daily life, outside the doctor’s office. Doctors, in turn, are given access to a much more accurate, prospective measurement of the phenotype of mental disorder: rather than a static cross-sectional measure that is not representative of what the patient experiences outside the doctor’s office, they now have access to the true phenotype of continuous and dynamic variation in response to environmental challenges in the flow of daily life, allowing them to not only prescribe treatments, but also life style alterations targeting challenging environments.

## PRECISION DIAGNOSIS IN CLINICAL PRACTICE

An example of contextual precision diagnosis is depicted in Figure 2. “Diagnosis” here refers to the visual display of causal relationships between symptoms and environment (in the example: stress) in the circuit. The circuit not only focuses on environment and symptoms, but also includes positive affective states, thus increasing therapeutic relevance.

Previous work has shown that contextual precision diagnosis is highly sensitive to longitudinal development



**Figure 2** Contextual precision diagnosis. Thicker lines indicate stronger associations. The (simulated) patient in this example did 6 days of experience sampling in order to determine circuit patterns of stress and mutually impacting mental states. The resulting causal circuit is depicted. A strong positive (black lines) feedback loop exists between positive states (relaxed and cheerful) and a negative (dotted grey lines) feedback loop exists between the opposite mental states of being cheerful and being paranoid. Stress occasions paranoia and impacts negatively on cheerfulness. Being relaxed helps reducing low mood and anxiety. Both cheerfulness and paranoia have a strong tendency to persist over time, increasing the probability of stable symptoms (18).

of phenotypes across definable stages; in that connection strength and connection variability between mental states differ in a predictable fashion across different stages of psychopathology (44). In addition, there is evidence that symptom circuit dynamics based on momentary assessment technology is sensitive to genetic variation and neural function (45-47), and can be used to predict dynamic transitions from a state of vulnerability to illness (48).

Contextual precision diagnosis is idiographic and sensitive to stages of psychopathology, replacing the need for nomothetic approaches that lack validity and practical utility (49). Finally, there is emerging evidence that the process of contextual precision diagnosis using ESM has therapeutic effects by itself (50-52).

## CONCLUSIONS

Although it may be useful to retain some of the higher order syndromal groupings, such as common mental disorder and severe mental disorder, the focus of contextual precision diagnosis is on the individual, neutralizing the forces of stereotyping and treatment irrelevance. The summary



presented above suggests that novel momentary assessment diagnostic systems delivering patient- and treatment-relevant information represent a welcome addition to the diagnostic toolbox in psychiatry.

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